Infection Exposures Early in Life and Increased Risk of Asthma

Respiratory viral infection early in life is associated with increased **risk of asthma**.

General Information	
Broad Focus Area	Asthma
Background and Justification	Respiratory tract infections have been linked with asthma for over 40 years, but the recent literature reflects the complex nature of this relationship. While some studies have suggested that early life infections protect against the development of allergy and asthma, others suggest that viral infections may promote allergic sensitization and the development of asthma.[1] Only a National U.S. study can provide the geographic, socio-economic, rural/urban, and ethnic/racial diversity to test this series of hypotheses. The influence of the exposures on immune expression and the expression of disease will change over time. Gene-by-environment interactions can only be tested with sufficient numbers in each ethnic/racial stratum.
Prevalence/ Incidence	Nine million children less than 18 years of age are estimated to have asthma.[2] Among children, it is the most common chronic illness.[3] The prevalence of asthma increased from 35 to 62 per 1,000 children aged 0 to 17 years between 1980 and 1996.[4] Respiratory syncytial virus (RSV) is the most frequent cause of bronchiolitis and pneumonia among children under the age of one year.[5] In a typical year, the average child will have between three and eight acute viral respiratory illnesses; these illnesses become complicated by bacterial infections in 5% to 13% of childhood cases.[6] Acute respiratory disease accounts for an estimated 90,000 hospitalizations and 4,500 deaths each year in U.S. infants and young children.[7]
Economic Impact	In 1997, the annual estimated cost of pediatric asthma in the US was $6.6 billion.[8] By 2002, the total cost of asthma was estimated at $14 billion.[9] The more severe forms of asthma account for a disproportionate amount of the total direct costs; one study estimated that less than 20% of asthmatics account for over 80% of the direct costs.[10] Asthma also poses a substantial and increasing public health burden in lost time from school and usual activities and in health care utilization.

Exposure Measures			**Outcome Measures**	
Primary/Child	Frequency of respiratory viral infection: - Medically-treated respiratory illnesses, vaccinations, medicine usage - Biological markers of infection (lymphocytes, antibodies, cytokines/ interleukins, inflammatory markers)		***Primary/Child***	Asthma: - allergic sensitization - airway reactivity - immune system function (e.g., lymphocytes, cytokines, IgE, interleukins)
Methods	- Blood samples at examination intervals - Interview/questionnaire for illnesses - Medical record capture		Methods	- Examination and interview by medical professional (e.g., skin sensitivity test) - Medical record capture - Blood samples

Life Stage	Periodic, birth through year 5		Life Stage	Periodic, birth through year 20

Important Confounders/Covariates	
Smoking	In utero exposure to tobacco associated with increased prevalence of asthma (OR = 1.8). ETS exposure associated with wheezing, but not physician diagnosed asthma.[11]
Family lifestyle factors	Crowded living conditions with more asthma triggers such as dust and cockroaches, lack of a regular source of health care, low income, are associated with higher risk of asthma.[12, 13]
Health care access	Poor health care access in inner cities, especially among African Americans and Hispanics, exacerbates the risk of viral infections contributing to asthma attacks and deaths. [14, 15, 16]
Child's history of non-respiratory viral illness	It will be important to understand the role that non-respiratory viral illnesses (e.g., gastrointestinal) play, since the total virus burden will affect the child's antibody status and subsequent risk of disease.

Population of Interest		Estimated Effect that is Detectable
All children		The smallest detectable relative risk is approximately 1.2. This power estimate assumes a sample size of 100,000 at age of diagnosis, an asthma incidence of 5%, and a cut-off value for "high" exposure based on the upper 5th percentile of NCS subjects (i.e., a proportion exposed of 0.05). It assumes only a main effects model based on exposure to a single factor (e.g., presence of a respiratory viral infection between birth and 24 months of age) without consideration of interactions with other exposures, genetics, family history, etc.[17]

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